FFT-P2 ^{161}Tb-OBELEŽENI BISFOSFONATI KAO POTENCIJALNI AGENSI ZA CILJANU RADIONUKLINDU TERAPIJU

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Terapija bisfosfonatima obeleženim β⁻-emitujućim radionuklidima se pokazala kao efikasna u palijativnom zbrinjavanju i kontroli koštanih metastaza. Cilj ove studije je bila priprema ^{161}Tb obeleženih bisfosfonata sa visokim prinosom, stabilnih u toku određenog vremena, i odgovarajuće biodistribucije.

Etidronat i zoledronat su obeleženi ^{161}Tb na sobnoj temperaturi (pH 7), dok je DOTA konjugovani bisfosfonat BPAMD obeležen ^{161}Tb na 95 °C, 30 minuta. Studije stabilnosti su sprovedene u fiziološkim uslovima. Test vezivanja za hidroksiapatit je *in vitro* metoda procene afiniteta ispitivanih kompleksa prema mineralnoj komponenti kosti. Studije biodistribucije sprovedene su na zdravim Wistar pacovima nakon intravenske primene, a radioaktivnost po organima izmerena je gama brojačem i izražena kao procenat radioaktivnosti po organu (%ID).

Radiohemijska čistoća određena ITLC metodom je bila preko 98% za sve komplekse. Bisfosfonati su pokazali odličnu stabilnost u fiziološkom rastvoru (>95%) i humanom serumu (>94%) tokom 48 časova. Test vezivanja za hidroksiapatit pokazao je izražen afinitet prema kostima (>98%). Biodistribucijom je utvrđeno brzo i izraženo nakupljanje u kostima, pri čemu je više od 60% injektovane aktivnosti izmereno u kostima dva sata nakon aplikacije. Nakupljanje u mekim tkivima je bilo minimalno sa brzom eliminacijom, što ukazuje na povoljan farmakokinetički profil i dugotrajnu retenciju u kostima.

Svi bisfosfonati pokazali su značajnu *in vitro* stabilnost, visok afinitet i zadržavanje u kostima, kao i minimalnu akumulaciju u ostalim organima. Dalja ispitivanja ^{161}Tb-obeleženih bisfosfonata na tumorskim modelima i poređenje sa ^{177}Lu obeleženim bisfosfonatima su neophodna kako bi se utvrdio njihov potencijal za ciljanu radionuklidnu terapiju.

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FFT-P2 ^{161}Tb-LABELED BISPHOSPHONATES AS POTENTIAL AGENTS FOR BONE-TARGETED RADIOTHERAPY

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Radiopharmaceutical therapy using bone-targeting agents labeled with β⁻-emitting radionuclides has proven effective for pain palliation and disease management. This study aimed to develop ^{161}Tb-labeled bisphosphonates with high radiolabeling yield, in vitro stability, and appropriate biodistribution.

Etidronate and zoledronate were radiolabeled with ^{161}Tb at room temperature (pH 7), whereas the DOTA- conjugated bisphosphonate BPAMD was labeled with ^{161}Tb under mild heating conditions (95 °C, 30 min). Stability studies were performed under physiological conditions. In vitro hydroxyapatite binding assays were conducted to evaluate mineral affinity. Biodistribution studies were conducted in healthy Wistar rats following intravenous administration, and radioactivity in excised organs was measured by gamma counting and expressed as percentage of the injected dose (%ID).

All radiocomplexes were obtained with radiochemical yields exceeding 98%, as confirmed by ITLC method. The compounds exhibited excellent stability in saline (>95%) and human serum (>94%) over 48 h. Hydroxyapatite binding studies demonstrated strong mineral affinity with high binding (>98%). Biodistribution studies revealed rapid and pronounced skeletal uptake, with more than 60% of the injected activity localized in bone within 2 hours post-injection. Uptake in soft-tissues and non-target organs was low and declined rapidly, indicating favorable pharmacokinetics and prolonged bone retention.

All bisphosphonates showed excellent in vitro stability and strong bone affinity with high skeletal uptake and low non-target accumulation. These results support further evaluation of ^{161}Tb-labeled diphosphonates in tumor-bearing models and comparative studies with established ^{177}Lu analogs, positioning them as strong candidates for bone-targeted radionuclide therapy.

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